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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,527	01/09/2002	George Stuart Cockerill	PU3743USW	4128

23347 7590 01/08/2004

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EXAMINER

TRUONG, TAMTHOM NGO

ART UNIT PAPER NUMBER

1624

DATE MAILED: 01/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicant(s) N .

10/030,527

Applicant(s)

COCKERILL ET AL.

Examiner

Tamthom N. Truong

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-43 is/are pending in the application.
- 4a) Of the above claim(s) 3, 23, 25, 28, 30, 33 and 35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4-12, 15-22, 24, 26, 27, 29, and 36-43 is/are rejected.
- 7) ☒ Claim(s) 13, 14, 31, 32, and 34 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☒ Interview Summary (PTO-413) Paper-No(s). 7.
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3. 6) ☐ Other:

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DETAILED ACTION

In applicant's response of 8-15-03, an election of group XII (claims 1, 2, 4-22, 24, 26, 27, 29, 31, 32, 34, and 36-43 (part of each)) was made with traverse. The traversal was on the ground that "an unduly burdensome search and examination" had not been established since the examiner had not shown (1) separate classification, (2) separate status in the art, or (3) a different field of search.

The traversal is not found persuasive for the following reasons:

- A. The restriction was done based on the criteria of "Lack of Unity" of PCT Rule 13.1. Therefore, there is no requirement to show separate classification, or separate status in the art.
- B. The requirement for Unity of Invention demands a common special technical feature. In the instant case, the common special technical feature is a ring having X=Y fused to pyrimidyl ring substituted with -N-Phenyl. Such a technical feature does not define the invention sufficiently, and does not contribute to the art. Depending on what X and Y represent, the bicycle of formula I varies from quinazoline to pyrido-pyrimidine. Furthermore, when either X or Y is CR¹, the special technical feature varies as Ar (in R¹) varies.
- C. The unduly burdensome search and examination exist as a separate on-line search is required for each group. This is evident by the extensive IDS submitted by applicant as well as the attached CAS printout for the search on a fused pyrimidyl ring substituted with an anilino.

However, in the interview of 8-19-03, the examiner agreed to combine some of the groups to reduce the restriction to 10 groups as follows:

- I. The combination of the original groups I, VI, and XI wherein Ar is **phenyl** in these groups;
- II. The same as the original group II wherein X is CR¹; Y is N; and Ar is furan;
- III. The combination of the original groups III, and V wherein X is CR¹; Y is N, and Ar is **thiophene or thiazole**;
- IV. The same as the original group IV wherein X is CR¹; Y is N, and Ar is **pyrrole**;
- V. The same as the original group VII wherein X is N; Y is CR¹, and Ar is furan;
- VI. The combination of the original groups VIII and X wherein X is N; Y is CR¹, and Ar is thiophene or thiazole;
- VII. The same as the original group IX wherein X is N; Y is CR¹, and Ar is pyrrole;
- VIII. The same as the original group XII wherein X is CR¹ or CR²; Y is CR¹ or CR², and Ar is furan;
- IX. The combination of the original groups XIII, and XV wherein X is CR¹ or CR²; Y is CR¹ or CR², and Ar is thiophene or thiazole;
- X. The same as the original group XIV wherein X is CR¹ or CR²; Y is CR¹ or CR², and Ar is pyrrole.

Applicant's election of the original group XII is equivalent to the new group VIII. Thus, claims 1, 2, 4-22, 24, 26, 27, 29, 31, 32, 34, and 36-43 (part of each) are considered herein while

claims 3, 23, 25, 28, 30, 33 and 35 are withdrawn from consideration as being drawn to the non-elected subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. **Lack of Written Description:** Claims 1, and 36-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 1, and 36-38 recite the limitation of “physiologically functional derivative” which does not have a description in the specification in terms of chemical structures, or conditions in which such a derivative is expected. On page 67, the specification merely provides an example of “*an ester, which upon administration to a mammal, ..., is capable of providing...such a compound or an active metabolite thereof.*” Such an example alone does not adequately describe the actual chemical structure of a “physiologically functional derivative”. It appears that the limitation of a “physiologically functional derivative thereof” includes both a ‘prodrug’ and an ‘active metabolite’. However, a ‘prodrug’ does not have the same meaning as an ‘active metabolite’.

For one thing, an 'active metabolite' only has a partial chemical structure of the parent compound while a 'prodrug' has additional ester or amide group that can be hydrolyzed *in-vivo*. Furthermore, the cleavage of such an ester or amide depends on its location on the parent compound. Without a description of the structure and location of such an ester or amide, one cannot be certain what constitutes a "physiologically functional derivative". Therefore, claims 1, and 36-38 lack written description, and so do the composition and method claims 39-43.

2. **Enablement:** Claims 1, and 36-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Because there is no description for a "physiologically functional derivative", one would have to research extensively to make such a derivative. For one thing, one would have to research for an ideal location of an ester or amide that could be readily hydrolyzed to release the parent compound. Since there is no common 'prodrug' or common 'active metabolite', one skilled in the art would have to carry out undue experimentation to make and use the claimed "physiologically functional derivative".

Double Patenting

The **nonstatutory double patenting** rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

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F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1, 2, 4-12, 15-22, 24, 26, 27, 29, 36, and 39-43 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, 4, 8, 10, 28, and 30-32 of U.S. Patent No. 6,391,874. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds of the instant formula (I) with Ar as furan, and R⁵ as an alkyl are embraced by the formula (I) of US'874 with X as N, Y as NR^b, and R¹ as furan substituted with M¹-M²-M³-M⁴.

The instant pharmaceutical composition and method claims also overlap with those of US'874 because the "disorder mediated by aberrant protein tyrosine kinase" would include cancer and psoriasis as well. Note the same type of protein tyrosine kinase is claimed in both instances.

Note, the instant compounds with either X or Y as N, and/or R⁵ as a substituted alkyl group, or a ring are not embraced the formula (I) of US'874.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1, 2, 4-12, 15-22, 24, 26, 27, 29, 36, and 39-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Cockerill et. al.** (US 6,391,874 or WO 98/02434). As discussed in the Obviousness-type Double Patenting rejection above, Cockerill et. al. disclose a genus of anilino-quinazoline that reads on the instant formula (I). Although the disclosed species (column 70, line 5) had been excluded from the instant claims, the preferred embodiment on column 9 of US'874 would have provided the express motivation for one skilled in the art to select the anilino-quinazoline compounds of the claimed formula (I). Note, in said preferred embodiment, R^1 is a 5- or 6- membered heterocyclic ring substituted with R^3 , which can be M^1 - M^2 - M^3 - M^4 . Variable M^4 can represent SO_2R^{13} which corresponds to the instant R^5 - SO_2 . Since R^{13} only represents hydrogen or C_{1-4} alkyl, it allows for a subgenus that is narrow enough for a prima facie case of obviousness.

Therefore, at the time of the invention, it would have been obvious to make anilino-quinazoline compounds as claimed herein and apply them in the treatment of a disorder mediated by aberrant protein tyrosine kinase activity.

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Claim Objections

5. Claims 13, 14, 31, 32, and 34 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Said claims recite anilino-quinazoline compounds wherein R⁵ is ring which is not taught by Cockerill et. al. (US'874 or WO'434).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 703-305-4485. The examiner can normally be reached on M-F (7 am -12 pm, and 3 pm - 6 pm) starting from 10-1st -03.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 703-308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.


Richard L. Raymond
Acting SPE
Art Unit 1624

T. Truong

January 5, 2004